II. REMARKS

Claims 1 to 20 are pending in the subject application. By this Amendment and Response, claims 1, 2, 4, 7, 14, 15, 20 and 29 have been have been amended and claims 18 and 19 have been canceled. Support for the amendments to the claims is found in the specification on page 6, lines 7 to 29. Accordingly, an issue of new matter is not raised by these amendments and entry thereof is respectfully requested.

The amendments to the claims and the addition of the new claims is not intended to be a dedication to the public of the claims as previously presented. Applicants respectfully reserve the right to file the same or similar claims in a related application.

In view of the preceding amendments and the following remarks, reconsideration and withdrawal of the outstanding rejections is respectfully requested.

Examiner Interview

Applicant and her attorney thank the Office for the courtesy extended to them during the March 28, 2005 telephonic interview. The independent claims were discussed and why the invention of these claims were not anticipated by the cited art. The rejections under 35 U.S.C. § 112, first paragraph also were discussed, and in particular, why the claims are enabled without a specific structural of an inhibitor. Although an agreement was not reached between the Office and Applicant, the interview clarified the issues remaining in the examination of the claims.

Claim Objections

Claims 18 to 20 stand objected to under 37 C.F.R. § 1.75(c) for allegedly being in improper dependent form for failing to limit the subject matter of a previous claim. The Office argued that claims 18 and 19 are directed to methods of treating a condition in a patient wherein the patient is suffering from a condition that is not an element of the main claim. The Office also noted that claim 20 appeared to be a duplicate of claim 11.

In reply to the objection, claims 18 and 19 have been canceled without prejudice or disclaimer. Claim 20 has been amended. In view of the cancellation of claims 18 and 19, and the amendment of claim 20, reconsideration and withdrawal of the claim objections is respectfully requested.

35 U.S.C. § 112, First Paragraph

Claims 1 - 20 were rejected under 35 U.S.C. § 112, first paragraph on the ground that the specification allegedly does not enable the full scope of the claims. The Office argued that the specification does not provide enablement for all matrix metalloproteinases (MMPs) because the use of this functional language allegedly does not apprise those of skill in the art of the compounds that would possess this function and that it would require an undue amount of experimentation to determine those compounds or agents that fall within the scope of the claim.

Applicant respectfully traverses. The use of functional language does not *ipso facto*, render claims unpatentable for failure to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph. *See, The Johns Hopkins Univ. v. Cellpro, Inc.*, 152 F.3d 1342, 47 U.S.P.Q.2d 1705 (Fed. Cir. 1998). In the case at issue, the term "matrix metalloproteinase inhibitor that inhibits up-regulation of MMP-9 and/or MMP-2 isoenzymes" defines a class of chemical compounds known to those of skill in the art at the time the application was filed. In support of this, Applicant has attached to this response copies of Whittaker, M Y.. et al. (1999) "Design and Therapeutic Application of Matrix Metalloproteinase Inhibitors" Chem. Rev. **99**:2735-2776; Tamara, Y. et al. (1998) "Highly Selective and Orally Active Inhibitors of Type IV Collagenase (MMP-9 and MMP-2): N-Sulfonylamino Acid Derivatives" J. Med. Chem. **41**:640-649 and Wada, C.K. et al. (2002) "Phenoxyphenyl Sulfone N-Formylhydroxylamines (Retroydroxyanates) as Potent Selectrive, Orally Bioavailable Matrix metalloproteinase Inhibitors" J. Med. Chem. **45**:219-232. Thus, it would not require an undue amount of experimentation to identify and use compounds falling with the scope of the claim and the claims meet the requirements of 35 U.S.C. §. 112, first paragraph.

In view of the above remarks and the attached publications, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

35 U.S.C. § 102

Claims 1-5, 9, 11, 12 and 18- 20 stand rejected as allegedly anticipated by Leitersdorf et al. (Clin. Nephrol, (1997) **48(1)**:48-51). The Office argued that the cited reference teaches administration of tetracyclines such as docycycline in amount of

about 100-600 mg/day to patients who have under gone liver transplantation and have developed nocardiosis. The Office argued that such patients are viewed to fall within the scope of the instantly claimed chemotherapy claims because such patients are immuno-suppressed. The Office stated that the subject claims are drawn to a process, and therefore, to be patentable the intended use of the claim must result in a manipulative differences as compared to the prior art. The Office alleged that since the method disclosed in the cited reference meets the administration step and the patient population of the instant claims, it would inherently achieve the process of the claims.

Applicant respectfully traverses. The cited reference teaches the administration of the antibiotic doxycycline to treat infectious disease. Although Applicant has discovered and now claims the use of doxycycline as an matrix metalloproteinase inhibitor, its prior use as an antibiotic does not anticipate because the antibiotic dosage is much lower that that required to inhibit a matrix metalloproteinase enzyme. For example, Applicant utilized an effective dose of 2100 mg/day of doxycycline in the study (assuming a 70 kg (154 lb) adult) which is well beyond the dose disclosed in the cited art.

Attached to this reply is Applicant's declaration that shows that a typical anti-infective dose of doxycycline (i.e., less than 15 mg/kg twice daily would not inhibit enzyme activity and therefore would not (and did not) inhibit MMP-2 or MMP-9 upregulation.

For these reasons, the rejection is improper and therefore should be removed.

35 U.S.C. § 103

Claims 6, 13 and 19 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Leitersdorf et al. The Office argued that absent unexpected results, it would have been obvious to one of ordinary skill in the art at the time of the invention would have been motivated to optimize the dosing frequency of Leitersdorf by routine experimentation.

Applicant respectfully traverses. It is a well-known axiom of patent law that that which is inherent in the prior art, if not known at the time of the invention, cannot form a proper basis for rejecting the claimed invention as obvious under § 103. *See In re Shetty*, 566 F.2d 81, 86, 195 U.S.P.Q. 753, 756-57 (C.C.P.A. 1977).

In *Shetty, supra,* the claims were drawn to certain adamantane compounds and a method of using them to curb appetite in animals. The prior art taught structurally similar compounds for use as antiviral agents, with recommended dosages that corresponded to those claimed by appellant. Agreeing with the Examiner that the prior art established a *prima facie* case of obviousness as to the composition, which Shetty did not rebut with any evidence of nonobviousness, the predecessor court to the Federal Circuit (CCPA) affirmed the rejection of the composition.

But the court did not affirm the Examiner's rejection of unpatentability regarding the method claims. Relying on prior art that taught antiviral activity rather than appetite curbing activity, the Patent Office had argued that administering the prior art compound in a dosage described in the art for antiviral effectiveness, which corresponded to appellant's appetite curbing amount, would inherently achieve appetite curbing and thus render the claimed method obvious. Refusing to accept this position, the Court responded that although Shetty's dosage "effective to curb appetite' corresponds to or inheres in [the prior art's] amount to 'combat microbial infestation' [,it] does not persuade us of the obviousness of appellant's method." *Id.* at 86, 195 U.S.P.Q. at 756. Before Shetty had discovered an appetite curbing effect for the claimed adamatane compounds, nothing in the art suggested using the structurally similar prior art adamantanes to curb appetite, much less the claimed dosage amount. Quoting from *In re Spormann*, 363 F.2d 444, 448, 150 U.S.P.Q. 449, 452 (C.C.P.A. 1966), the Court stated:

> [T]he inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown.

In re Shetty, 566 F.2d at 86, 195 U.S.P.Q. at 757. *See also In re Naylor*, 369 F.2d 765, 768, 152 U.S.P.Q. 106, 108 (C.C.P.A. 1966)("[Inherency] is quite immaterial if...one of ordinary skill in the art would not appreciate or recognize the inherent result.").

Accordingly, reconsideration and withdrawal of the rejections of the claims under 35 U.S.C. § 103 is respectfully requested.

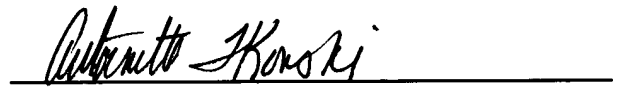
III. CONCLUSION

If the Examiner determines that a telephonic interview would advance prosecution of the application, the Examiner is invited to telephone Antoinette Konski at (650) 849-4950.

If the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-2518**, referencing no. 7000692001. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

DATE: June 8, 2005

Respectfully submitted,



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